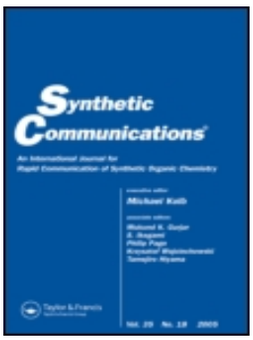

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AN EFFICIENT BIOMIMETIC CLEAVAGE OF *GEM*-DIACETATES TO ALDEHYDES BY β-CYCLODEXTRIN UNDER NEUTRAL CONDITIONS IN AQUEOUS MEDIUM*

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ABSTRACT

The cleavage of *gem*-diacetates to aldehydes, a widely used protecting group in organic synthesis, has been achieved for the first time under neutral conditions in aqueous medium using β-cyclodextrin as catalyst. The main advantage of the present methodology is that it can be used with compounds having a variety of functional groups since the cleavage is carriedout under neutral conditions in aqueous medium.

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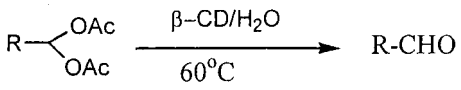
Selective protection and deprotection of carbonyl groups are of great significance in organic synthesis especially in multistep synthesis of natural products.[1] Amongst various protecting groups, *gem*-diacetates have been recognized as the method of choice due to their easy installation and removal and their stability in a variety of reaction conditions. Apart from this, these *gem*-diacetates are useful synthetic intermediates in various organic transformations.[2,3] However, most of the general methods used for the cleavage of these diacetates include various acidic reagents such as K10 clay,[4] hydrochloric acid,[5] sulfuric acid,[6] BI_3-*N*,*N*-dimethyl aniline complex[7] etc. as well as basic reagents such as sodium and potassium hydroxide.[8] However, these are some severe limitations with the literature methods such as use of strong acidic or basic conditions, lower yields, longer reaction times etc. Keeping in view the limitations of the existing procedures, we felt the need to develop an alternate and mild approach under neutral conditions using water as the solvent, which is an environmentally benign one. In our effort to develop biomimetic approaches for chemical reactions involving cyclodextrins in water,[9] we report herein, for the first time, a practical and efficient method for the cleavage of *gem*-diacetates to aldehyde catalysed by β-cyclodextrin under neutral conditions in aqueous medium.

Cyclodextrins (CDs) which are cyclic oligosaccharides with hydrophobic cavities exert microenvironmental effect leading to selective reactions. They catalyse reactions involving supramolecular catalysis through non-covalent bonding as seen in enzymes. These biomimetic reactions can be effectively carried out in water under neutral conditions without generating any toxic waste products. Thus, mimicking of biochemical selectivity which involves supramolecular catalysis with the reactions being carried out in water will be superior to chemical selectivity. This has prompted us to attempt the cleavage of *gem*-diacetates using CDs, as this is one of the most useful synthetic transformations (scheme).



R= aromatic, aliphatic and heterocyclic

Scheme.

The reactions were carried out by dissolving β-cyclodextrin in water followed by the addition of *gem*-diacetate. The yields of the products were

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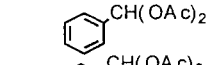
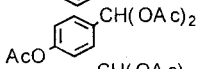
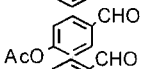
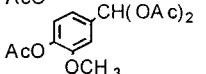
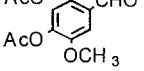
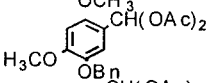
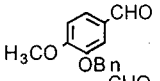
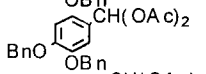
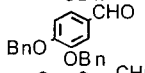
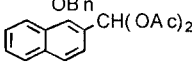
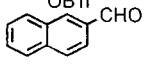
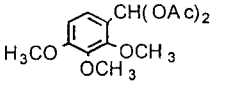
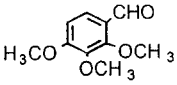
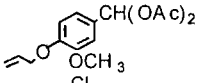
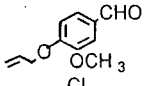
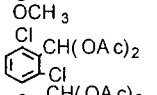
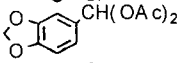
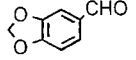
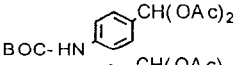
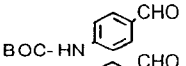
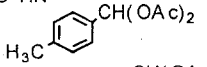
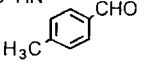
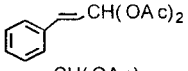
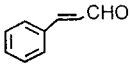
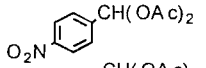
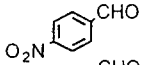
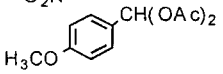
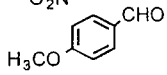
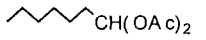
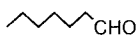
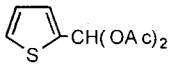
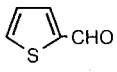
Table 1. Selective Cleavage of *gem*-Diacetates to Aldehydes Catalysed by β-Cyclodextrin

Entry	Substrate	Product[a]	Reaction Time(h)	Yield (%)[b]
1			6	95
2			6	88
3			6	89
4			7	85
5			8	80
6			7	89
7			8	80
8			8	80
9			8	72
10			7	92
11			8	70
12			6	89
13			6	80
14			8	71
15			6	90
16			8	60
17			6	65

a: All the products were characterised by ^{1}H NMR, IR and Mass Spectroscopy
b: Isolated Yields after purification.

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impressive (up to 95%) and these reactions can be efficiently carried out with only catalytic amount of cyclodextrin (0.1 mole of CD per mole of the substrate). The cyclodextrin can also be recovered and reused. These reactions do no take place in the absence of CD. This methodology apart from having the advantage of neutral conditions and aqueous medium is also compatible in the presence of various other functional groups such as *O*Me, *O*-Bn, *O*-Allyl, methylene dioxy, *O*Ac and *N*-Boc. However, the yields with aliphatic and heterocyclic *gem*-diacetates, are comparatively lower. Here, the role of CD appears to be to activate the acetyl group by hydrogen bonding, thus facilitating its cleavage in the presence of water. Though, this reaction takes place in the presence of α-CD also, β-CD will be the most preferred catalyst due to its easy accessibility and economic viability.

In conclusion, this biomimetic methodology is the first of its kind to be applied for the cleavage of *gem*-diacetates, one of the most commonly used protecting groups in organic synthesis, under neutral conditions in aqueous medium in the presence of β-cyclodextrin. This method is also compatible in the presence of other functional groups.

EXPERIMENTAL

^{1}H NMR spectra were recorded on Gemini-200 MHz spectrometer and mass spectra were observed on VG Autospect M. The IR spectra were recorded on NICOLET FT-IR. Spectrometer.

General Procedure for the Cleavage of *gem*-Diacetates in Aqueous Medium Using β-Cyclodextrin: In a typical procedure, to β-cyclodextrin (0.1 mmol) dissolved in 20 ml of water by heating at 60°C, was added *gem*-diacetate (1 mmol) in methanol (1 ml) and stirred at this temperature for the required length of time (table). The reaction mixture was cooled to room temperature and extracted with ethylacetate (3 × 20 ml). The combined organic extract was washed with water (2 × 10 ml), dried over anhydrous sodium sulphate and evaporated under reduced pressure to give the product. This was further purified by column chromatography on silica gel (100–200) using hexane: ethylacetate (90:10). The yields were in the range of (60–95%).

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